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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/762,767	06/01/2001	Harald Schmidt	VOS-101	7502

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EXAMINER

RAO, MANJUNATH N

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 03/31/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<p align="center"><b>Office Action Summary</b></p>	<b>Application No.</b> 09/762,767	<b>Applicant(s)</b> SCHMIDT ET AL.	
	<b>Examiner</b> Manjunath N. Rao, Ph.D.	<b>Art Unit</b> 1652	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 18 January 2004.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-13 is/are pending in the application.
- 4a) Of the above claim(s) 9-13 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-8 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \* c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |   |  |
|---|--|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)<br>2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)<br>3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____<br>5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)<br>6) <input type="checkbox"/> Other: _____ |
|---|--|

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### **DETAILED ACTION**

Claims 1-13 are currently pending in this application. Claims 1-8 are now under consideration. Claims 9-13 remain withdrawn from consideration as being drawn to non-elected subject matter.

Applicants' amendments and arguments filed on 1-8-04, have been fully considered and are deemed to be persuasive to overcome the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. Specifically Examiner has withdrawn the rejections under 35 U.S.C. 112, 2<sup>nd</sup> paragraph in view of claim amendments.

### ***Priority***

Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). The foreign priority document is German language. In order to perfect the foreign priority, applicants are urged to submit an English language translation of the same.

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Giuili et al. (FEBS Lett, Vol. 304(1):83-88). This rejection is based upon the public availability of a printed

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publication more than one year prior to the date of application for patent in the United States.

Claim 1 of the instant application is drawn to isolated human soluble gluanylyl cyclases  $\alpha$  1 or  $\beta$  1 subunits having the amino acid sequences SEQ ID NO:1 and 4 respectively purified to apparent homogeneity. Giuli et al. disclose isolated human soluble gluanylyl cyclases  $\alpha$  1 or  $\beta$  1 subunits having the amino acid sequences SEQ ID NO:1 and 4 respectively purified to apparent homogeneity. Thus Giuli et al. anticipate claim 1 of this application as written.

In response to the previous Office action, applicants have traversed the above rejection arguing that the rejection was unwarranted because the  $\alpha$  chain reported by Giuli et al. is not the same as that claimed in the instant claims. Applicants also argue that the amino acids of  $\alpha$  2 subunit reported by Giuli et al. includes 717 amino acid residues as opposed to 690 amino acids of SEQ ID NO:2 and that the sequence differs from SEQ ID NO:2 beginning with amino acid residue 124 to the end of the sequence. Examiner respectfully disagrees with the above arguments as being persuasive to overcome the above rejection. This is because Examiner has found a 100% match between the sequences claimed and the sequences depicted in the reference. See enclosed sequence alignments. It is not clear to the Examiner as to how applicants have concluded that the sequences in the reference and that claimed differ in such drastic manner as argued in their response. Therefore, in view a clear 100% sequence match, the above rejection is maintained.

Claims 1 and 2 are rejected under 35 U.S.C. 102(a) as being anticipated by Zabel et al. (Biochem J., Vol. 335(1):51-57, October 1, 1998). This rejection is based upon the public availability of a printed publication in the United States. Claims 1 and of the instant application

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is drawn to isolated human soluble gluanylyl cyclases  $\alpha$  1 or  $\beta$  1 subunits having the amino acid sequences SEQ ID NO:1 and 4 respectively purified to apparent homogeneity and a method of producing the subunits by expressing the polynucleotide encoding the subunits in prokaryotic or eukaryotic host cells and obtaining the subunits. Zabel et al. disclose isolated human soluble gluanylyl cyclases  $\alpha$  1 or  $\beta$  1 subunits having the amino acid sequences SEQ ID NO:1 and 4 respectively purified to apparent homogeneity as well as a method of making said polypeptides by expressing the polynucleotides encoding said subunits in eukaryotic host cells such as insect cells. Thus Zabel et al. anticipate claims 1 and 2 of this application as written.

In response to the previous Office action, applicants have traversed the above rejection arguing that the rejection was unwarranted as Zabel et al. reference has a publication date of October 1, 1998 which is after the filing date of the priority application and that the reference contains the work of the present inventors published less than one year before filing the PCT application from which the present application claims priority. While Examiner agrees with the applicants that the reference is post dated to the foreign priority and is the work of present inventors, the reference continues to anticipate instant claims because of the following reasons. The foreign priority document is in a language other than English and applicants have not filed a translation of the same such that Examiner can determine that the foreign priority document has ample support for the claimed subject matter. Next, the inventive entity of the reference is different from that of the instant application. Therefore, the above rejection is warranted and therefore maintained. A Declaration filed 37 CFR 1.132 and an English language translation of the priority document would overcome the above rejection provided Examiner can determine that the foreign priority document has ample support for the instant claims. See MPEP 716.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 3-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Zabel et al. or Giuli et al. as applied to claims 1 or 2 or 1 and 2 above, and further in view of the common knowledge in the art regarding the methods of affinity chromatography using affinity tags for protein purification. Claims 3-8 are directed to methods of producing soluble human guanylyl cyclases (sGC) wherein the step of obtaining the subunits comprises a lysis of cell followed by affinity chromatography of the cell lysate and subsequent elution of the subunits, wherein the expression vectors contains at least one additional DNA sequence encoding for a domain for the specific chromatography (affinity tag) with appended protease cleavage site, wherein the sGC comprises either or both subunits linked to the tag (as in claim 5-8).

The references of Giuli et al. and Zabel et al. has already been discussed above. Both references provide the cDNA expressing the above protein subunits. Zabel et al. also teach the expression of the proteins in a eukaryotic host cell followed by its extraction by cell lysis. However, both references do not teach the affinity chromatography technique for the purification of the above proteins.

The art is rich in teachings of recombinant protein purification techniques involving tags such as histidine tags. In fact, several commercial protein purification kits with appropriate kits are available in the art for those interested in making purified recombinant proteins.

Therefore, with the cDNA for the above sGC enzyme provided by the above two references it would have been obvious to those skilled in the art to subclone the cDNAs provided by the two references in any convenient expression systems which make use of tagged sequences and produce the polypeptides as claimed in claims 3-8. One of ordinary skill in the art would have been motivated to do so as both the above references teach the important role played by the enzyme in signal transduction. One of ordinary skill in the art would have a reasonable expectation of success since the above two references provide a cDNA and the art provides mechanisms to make and express the polypeptide as required.

Therefore, the above invention would have been *prima facie* obvious to one of ordinary skill in the art.

Applicants have traversed the above rejection as unwarranted in view of their claim that the references of Giuili et al. and Zabel et al. are not valid anticipating references. Examiner respectfully disagrees with such an argument. Examiner urges applicants to review the rejections under 35 U.S.C. 102 § above wherein Examiner has shown that the references are valid anticipating references. Therefore, the above rejection is maintained.

### ***Conclusion***

None of the claims are allowable.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

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MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Manjunath N. Rao, Ph.D. whose telephone number is 703-306-5681. The examiner can normally be reached on 7.30 a.m. to 4.00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 703-308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-306-0196.



Manjunath N. Rao  
March 25, 2004